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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/730,495	12/05/2003	Richard B. Borgens	3220-73828	2575

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/730,495	BORGENS ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 18-27* is/are pending in the application.

4a) Of the above claim(s) *3 and 4* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This is an RCE of SN 10/730,495.

Claims 1-2, 5-17 have been canceled. New claims 18-27 are pending.

2. Applicants attention is drawn to that upon restriction between an invention of chemical products i.e. compounds and its method of using i.e. method of treating injured nervous tissue, the rejoinder are granted when *the compounds have been found to be novel and unobvious.*

Advisory of a Rejoinder

The following is a recitation of MPEP 821.04, Rejoinder:

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. See MPEP § 806.05(f) and § 806.05(h). The claims to the nonelected invention will be withdrawn from further consideration under 37 CFR 1.142. See MPEP § 809.02(c) and § 821 through § 821.03. However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.
> Where the application as originally filed discloses the product and the process for making and/or using the product, and only claims directed to the product are presented for examination, when a product claim is found allowable, applicant may present claims directed to the process of making and/or using the patentable product by way of amendment pursuant to 37 CFR 1.121. In view of the rejoinder procedure, and in order to expedite prosecution, applicants are encouraged to present such process claims, preferably as dependent claims, in the application at an early stage of prosecution. Process claims which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance. Amendments submitted after final rejection are governed by 37 CFR 1.116. Process claims which do not depend from or otherwise include the limitations of the patentable product will be withdrawn from consideration, via an election by original presentation (see MPEP § 821.03). Amendments submitted after allowance are governed by 37 CFR 1.312. Process claims which depend from or otherwise include all the limitations of an allowed product claim and which meet the requirements of 35 U.S.C. 101, 102, 103, and 112 may be entered. *Applicants are reminded of propriety of process of use claims in consideration of the "reach-trough" format which is drawn to mechanistic, receptor binding or enzymatic functionality. Reach through claims are considered lacking of descriptive and enabling support from the specification. Thus, rejoinable process of use claims are those with particular disease named with efficacy support from the specification for treating the particular disease.*
>
> Where product and process claims are presented in a single application and that application qualifies under the transitional restriction practice pursuant to 37 CFR 1.129(b), applicant may either: (A) elect the invention to be searched and examined and pay the fee set forth in 37 CFR 1.17(s) and have the additional inventions searched and examined under 37 CFR 1.129(b)(2); or (B) elect the invention to be searched and examined and not pay the additional fee (37 CFR 1.129(b)(3)). Where no additional fee is paid, if the elected invention is directed to the product and the claims directed to the product are subsequently found patentable, process claims which either depend from or include all the limitations of the allowable product will be rejoined. If applicant chooses to

pay the fees to have the additional inventions searched and examined pursuant to 37 CFR 1.129(b)(2) even if the product is found allowable, applicant would not be entitled to a refund of the fees paid under 37 CFR 1.129(b) by arguing that the process claims could have been rejoined. 37 CFR 1.26(a) states that "[T]he Commissioner may refund any fee paid by mistake or in excess of that required. A change of purpose after the payment of a
fee...will not entitle a party to a refund of such fee..." In this case, the fees paid under 37 CFR 1.129(b) were not paid by mistake nor paid in excess, therefore, applicant would not be entitled to a refund. In the event of rejoinder, the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101,102, 103, and 112. If the application containing the rejoined claims is not in condition for allowance, the subsequent Office action may be made final, or, if the application was already under final rejection, the next Office action may be an advisory action.

The following is a recitation from paragraph five, "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. 103(b)" (1184 TMOG 86(March 26, 1996)):

"However, in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim **depends from or otherwise includes all of the limitations of** an allowed product claim. Withdrawn process claims not commensurate in scope with an allowed product claim will not be rejoined." (emphasis added)

Therefore, in accordance with MPEP 821.04 and In re Ochiai, 71 F. 3d 1565, 37 USPQ 1127 (Fed. Cir. 1995), rejoinder of product claims with process claims commensurate in scope with the allowed product will occur following a finding that the product claims are allowable. Until, such time, a restriction between product claims and process claims is deemed proper. Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution to maintain either dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Please note that none of the compound claims have been found to be novel and unobvious. In addition applicants have canceled all the compound claims. Therefore, the newly amended and added claims are subject to the following restriction:

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 3-4, drawn to pharmaceutical composition, classified in class 514, subclass various, depending on species election. If this group is elected, a further election of a single disclosed species is also required and further restriction based on the elected species with respect to the core structure will be required.

II. Claims 18-24, 27, drawn to method of treating mammalian nerve tissue, classified in class 514, subclass various depending on species election. If this group is

elected, a further election of a single disclosed species is also required and further restriction based on the elected species with respect to the core structure will be required.

III. Claims 25-26, drawn to method of treating injured nervous tissue with multiple active ingredients, classified in class 514, subclass various, depending on species election. If this group is elected, a further election of a single disclosed combination using multiple active ingredients with each element explicitly identified is also required and further restriction based on the elected combination may be required.

The inventions are independent or distinct, each from the other because:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the product of group I can be used in materially different process such as CA 112:193716 compounds anticipating the claims having anticytokinin activity i.e. obvious over composition containing such for anticytokinin use; or CA 127:161747 compounds anticipating the claims having found mutagenic activity i.e. obvious over composition containing such for food mutagenic use.

The method of using single active ingredient and the method of using multiple active ingredient is not related since the activity of a multiple active ingredient process does not depending on any single active ingredient but the combination and interaction of the multiple active ingredients.

During a telephone conversation with Mr. Blodgett on Mar 14, 2006 a provisional election was made with traverse to prosecute the invention of group II, claims 18-27. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-4, 25-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. Claims 18-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, as well as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention and/or the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In the specification, insufficient antecedent for the claims wherein R3-R6 forms rings other than 1H-imidazo[4,5-c]pyridine-2-one ring as disclosed on page 34, when R3 is POR4R5 or OR groups, or salts or solvates thereof. Please note that the scope of the claims being drawn to enormous ring size and chemical structure wherein starting material and their activity being analogous to the 4-aminopyridinyl compounds have not been described or nexus of activity being made of record. Further, no description of what kind of salts or solvates would have analogous activity with the base compounds. Although acid addition salts can be formed by mere mixing of the free base with a free acid, not information on what kind of solvates would be encompassed and how it is formed.

Especially, a survey of the prior art indicated that the phosphates or oximes have been known to be useful in synthesizing other material, no nexus can be found that such compounds having biological activity. The specification while provided limited information as to the biological activity of 4-substituted amino pyridinyl compounds disclosed on pages 33-34, the specification provided none of the phosphates or oximes having such activity (see CA84:74052, CA 59:9108; CA101:23604). Especially, phosphates have been well recognized in the chemical art to be extremely toxic, i.e. useful as nerve gas (see Wilbraham p.268-269).

In absence of specific description and enablement, the support for the scope of the claims are insufficient.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 18-24, 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shi et al. CA 126:258964, Greensmith et al. CA 124:136369, or references (Blight, Seil, Hays, Hansebout etc. recited in the specification p.3) recited on page 3 of the specification in view of Bundgaard, Gardner or Pop.

Determination of the scope and content of the prior art (MPEP §2141.01)

Shi et al. CA 126:258964, Greensmith et al. CA 124:136369, or references (Blight, Seil, Hays, Hansebout etc.) recited on page 3 of the specification disclosed explicitly that 4-aminopyridine is a well known compound having activity in restoration of action potential conduction through spinal lesions.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art method is the use of an N-acylated 4-aminopyridine instead of the amino pyridine. Bungaard taught that N-acylation is a prodrug design for amino containing drugs. Gardner taught that prodrug of hydrophilic drug such as amino containing compounds, upon change the hydrophilic-lipophilic balance can permit permeation of the drug to the cerebra spinal compartment. Thus, prodrug modification such as acylation would enhance lipophilicity thus enhance crossing of blood and brain barrier (see p. 659 last paragraph). Pop disclosed amino containing drugs with enhancement of delivery to the CNS compartment by acylated prodrug and taught the expected targeting operability (p.659, left column second paragraph).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The above references placed the active compound, the prodrug design and the expectation of such prodrug modification in the possession of artisan in the field. One having ordinary skill

in the field knowing the problem of the active compound (see specification of problem of the field p.3-4), would be motivated to make such modification of the active compound in the prior art with an acylation prodrug **because** artisan in the field is in possession of the skill for modification as recited above; the expectation of such modification would render a higher delivery into the cerebra spinal compartment i.e. wherein the activity is required, thus, expects a lessening of the distribution in the systemic circulation i.e. wherein the side-effects are avoided. Thus, the motivation, the skill and the expected results are well within the teaching of the art as a whole which rendered the instant methods prima facie obvious in absence of unexpected results.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Mar. 14, 2006

Celia Chang
Primary Examiner
Art Unit 1625